EXPERIMENTAL ANTICANCER STUDIES

Part 19. Anticancer Activity of 2-[(5-Nitro-2-furyl) vinylene]quinoline Carboxylic Acid-(4)*

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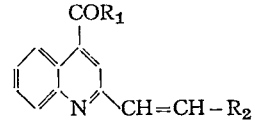
Since 1954, the investigators of our laboratory have been devoted themselves to the anticancer studies with a number of derivatives of 2,2'-dihydroxyazobenzene[1,2], Schiff base type[3,4] and aminoalkylresorcinol[5].

In the course of the study, ten compounds of following type of chemical constitutions were also synthesized and tested for their anticancer activity.



Each of seven 2-substituted quinoline carboxylic acid-(4) derivatives was obtained by condensation of 2-methylquinoline carboxylic acid-(4) with the respective aromatic aldehyde in the presence of acetic anhydride or zinc chloride, according to the method described by Royer[6]. Three hydrazides of 2-substituted quinoline carboxylic acid-(4) were prepared by acting hydrazine on each of 2-(styryl), 2-(*p*-aminostyryl) and 2-(*p*-dimethylaminostyryl)quinoline carboxylic acid-(4) esters. All these compounds were shown to be of *trans* configuration.

The results so far obtained in the anticancer experiments, in which each mouse was given intraperitoneally a daily dose of 1/5 LD_{50} of a test compound for seven successive days after inoculation of Ehrlich carcinoma cells, are as follows : Among ten compounds, 2-[(5-nitro-2-furyl) vinylene]quinoline carboxylic acid-(4) (No.256) was found to be most effective in causing prolongation of the life-span of mice bearing Ehrlich ascites carcinoma (Table 1). It was also observed that the growth of solid form of the carcinoma was moderately inhibited by the compound (Table 2).

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* See Juzen Igk. Z., **69** (3), 1963 (in press).

Here should be noted is the matter that while this paper was in manuscript, it was reported[7], on December 7, 1963, by K. Miura and co-workers of the Faculty of Pharmacy, Kanazawa University that 2-[(5-nitro-2-furyl)vinylene]quinoline carboxylic-(4) was also tested to be effective against Ehrlich carcinoma in mice.

Further work is in progress.

The author wishes to express thanks to the members of Faculty of Pharmacy, Kanazawa University for elemental and spectral analyses.

REFERENCES

1) **Okamoto, H., Koshimura, S., Hirata, R., Murasawa, K., Bando, Y. & Shimizu, R.** : Z. Krebsforsch., 62, 408, 1958.

2) **Koshiura, R., Kagotani, Y., Murakami, N., Kirita, T. & Sato, I.** : This Journal, 19 (3), 231, 1962.

3) **Koshiura, R., Kagotani, Y. & Ujiie, T.** : Chem. Pharm. Bull., 10, 528, 1962.

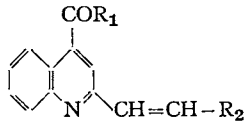
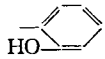
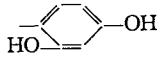
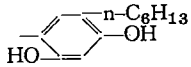
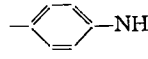
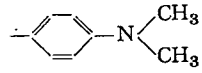
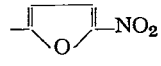
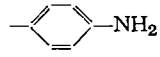
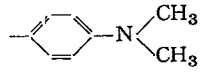
4) **Ujiie, T.** : unpublished.

5) **Koshiura, R. & Kagotani, Y.** : This Journal, 21 (1), 85, 1963.

6) **Royer, R.** : J. Chem. Soc., 1949, 1803.

7) Presented at the 41th Meeting of the Jūzen Medical Society (Kanazawa) on December 7, 1963.

Table 1.
2-Substituted quinoline carboxylic acid-(4) derivatives and their action on Ehrlich ascites carcinoma in mice

No.	Compound	Dose	Anticancer activity :
		(mg/kg/day) × 7 (i.p.)	Number of survivors/test animals after 50 days of inoculation*
	R_1 R_2		
250	OH 	100	0/10
251	OH 	100	2/10
252	OH 	40	0/10
253	OH 	50	2/10
254	OH 	5	0/10
255	OH 	300	0/ 5
256	OH 	25	8/10
257	$NHNH_2$ 	35	0/10
258	$NHNH_2$ 	25	0/10
259	$NHNH_2$ 	25	0/10
	Mitomycin C	1	10/10
	Control	•	0/10

* Each animal was inoculated intraperitoneally with 4×10^6 Ehrlich ascites carcinoma cells. The treatment with agents was initiated 24 hours after inoculation.

Table 2.

Effect of No. 256 on solid form of Ehrlich carcinoma in mice

	Treated groups		Control group
	No. 256 (0.5mg/mouse/day) ×7	Mitomycin C (20μgm/mouse/day) ×7	
Weight of tumor (gm)	0.572	0.387	1.334
	0.444	0.240	1.102
	0.343	0.235	0.834
	0.303	0.215	0.594
	0.301	0.214	0.509
	0.298	0.207	0.407
	0.247	0.173	0.406
	0.231	0.173	0.379
Mean (gm)	0.343	0.231	0.695
% Growth	49	33	100